

Serial No.: 09/830,666  
Atty. Docket No.: P66606US0

IN THE SPECIFICATION:

On page 1, please replace the title on line 1 with the following title:

--Method to Control an Overactive Bladder--.

On page 1, line 2 after the title, please insert the following headings:

--BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION--

On page 1, line 10, please insert the following heading:

--2. DESCRIPTION OF THE RELATED ART--.

On page 1, please replace the fourth full paragraph beginning on line 25 through page 2, line 3 with the following amended paragraph:

--The storage phase of the micturition cycle requires a stable bladder with high compliance (i.e. a relaxed bladder) and closed urethral outlet. However, due to the feedback system the bladder may easily become unstable. Any stimulus that elicits a small burst of impulses in the mechanoreceptor afferents, such as coughing and jumping, may trigger an involuntary micturition reflex and cause urine leakage. To prevent this from happening, the neural

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B2  
control system is equipped with several inhibitory circuits, both at spinal and supraspinal levels, which prevent the detrusor muscle to contractfrom contracting. However, these inhibitory circuits are susceptible to a variety of neurologic disorders. Therefore, patients with neurologic disorders frequently suffer from urinary incontinence due to involuntary detrusor contractions.--

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On page 2, please replace the second full paragraph with the following amended paragraph:

B3  
--Bladder inhibition by electrical stimulation has been described before [e.g. Vodúšek et al., 1988; Wheeler et al., 1992] but only continuescontinuous stimulation was used, e.i.—i.e. stimulation is permanent except during voiding.--

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On page 2, please delete lines 20-30 in their entirety.

B4  
On page 2, line 31, please insert the following heading:  
--SUMMARY OF THE INVENTION--.

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On page 2, please replace line 32 with the following amended line 32:

--The objectobjects of the inventionsisinvention are--.

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On page 3, please replace the third and fourth paragraphs, beginning at line 10 through the first full paragraph on page 4, ending at line 20, with the following amended paragraphs:

--Treatment of detrusor overactivity and

*P 5*

~~extimation~~~~estimation~~ of bladder volume can be achieved by a method as described in the first paragraph using a closed loop stimulation system to allow ~~event driven~~~~event-driven~~ inhibition of the bladder where stimulation is only applied when an undesired bladder contraction occurs, and an implanted sensor comprising at least one nerve electrode to sense electrical signals from nerves innervating the bladder. Sensing electrical signals related to mechanical bladder activity via said sensor, ~~and detecting~~~~the method detects~~ the onset of a bladder contraction and ~~estimation of~~~~estimates~~ bladder volume using signal processing methods, ~~and activating~~ an inhibitory neural circuit by stimulating afferent nerve-fibbers, in ~~response to detection of the onset of a bladder contraction fibers.~~

By this method no nerves ~~has~~~~have~~ to be cut, and no irreversible surgery has to be done. Stimulation of neural tissue only takes place when needed, and the volume of the bladder is monitored. The present invention uses electrical stimulation to inhibit the bladder. Inhibition of the bladder by electrical stimulation is possible since, besides the mentioned neural

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inhibitory circuits, additional spinal inhibitory circuits exist to prevent involuntary leakage during, e.g., defecation, coitus and physical activity. Activation of the afferent ~~path~~paths of these neural circuits has two effects: they activate the inhibitory sympathetic ~~neurones~~neurons to the bladder and they provide central inhibition of the preganglionic detrusor-motoneurons through a direct route in the spinal cord. These additional inhibitory reflexes are not suppressed during micturition, which means that they are quite capable of interrupting a detrusor contraction. Activation of these reflexes by electrical stimulation is a nondestructive alternative method for patients who are refractory to drugs, cannot tolerate the side effects or for other reasons do not accept a drug treatment.

~~Primarily~~Primarily, the recorded nerve signals comes come from afferents innervating mechanoreceptors located in the bladder wall. By detecting the onset of the bladder contraction, the stimulator ~~could~~can be activated only when contraction occurs, and ~~continuos~~continuous stimulation is not necessary. This minimises the risk of neural ~~damages~~damage due to the stimulation. In addition, if the patient can sense the stimulation, the duration of stimulation should be minimised to minimise the discomfort.--

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On page 4, please replace the third full paragraph beginning at line 27 with the following amended paragraph:

--The step of implanting a sensor might comprise the step of implanting an intrafasicular electrode [Lefurge et al., 1991]. The intrafasicular electrode is flexible and ~~smaller~~small, and ~~might~~may be preferred in locations where limited space is available.--

On page 5, please replace the second paragraph beginning at line 7, with the following amended paragraph:

--The electrode can be located at the intradural or extradural dorsal sacral nerve roots. In this way the electrodes can be placed at a ~~mechanical~~mechanically stable position, and the nerve roots are relatively long, which enables easy placement of electrodes.--

On page 5, please replace the fourth paragraph beginning at line 17, with the following amended paragraph:

--The electrode can be located at the intradural or extradural ventral sacral nerve roots. In this way the electrodes can be placed at a ~~mechanical~~mechanically stable position, and the nerve roots are relatively long, which enables easy placement of electrodes.--

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On page 5, please replace the sixth paragraph beginning at line 29, with the following amended paragraph:

B9  
--Preferably two different nerve signals can be used to detect a detrusor contraction, where the first signal comes from afferent nerves innervating the bladder, and the second signals signal comes from efferent nerves innervating the detrusor muscle. In this way the detrusor contraction can be detected more-reliable reliably.--

B10  
On page 6, please replace the third and fourth paragraphs beginning at line 13, with the following amended paragraphs:

--The bladder volume can be derived from the time between 2two consecutive detrusor contractions. By measuring of the bladder volume, the patient can be informed about his/her bladder volume.

The bladder volume can be derived form from both the amplitude of the recorded nerve signal and the time between 2two consecutive detrusor contractions. This way the bladder volume can be estimated in a more reliable way.--

On page 6, before line 25, insert the following heading,  
--BRIEF DESCRIPTION OF THE DRAWINGS--.

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On page 6, line 33, insert the following heading along  
with the paragraph following thereafter:

--DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Further scope of applicability of the present invention will become apparent from the detailed description given hereinafter. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.--.

On page 6, please replace the ninth paragraph beginning at line 34 through page 7, line 28, with the following amended paragraph:

--Mechanoreceptors located in the bladder wall act as tension receptors and respond in graded fashion to increases in bladder volume and intravesical pressure-[Sengupta and Gebhart, 1994]. It has been shown that a close relationship between afferent nerve activity and the pattern of intravesical pressure changes is best observed when the activity of many afferent nerve fibres is summed. Sensor 14 comprises an implantable nerve cuff electrode. This type of electrode surrounds the selected nerve in close

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proximity so currents generated by the nerve fibres result in sufficient sufficiently large voltage differences in the volume within the cuff so that they can be detected by the electrode. However, other electrode configurations such as intrafasicular electrodes could also be used to detect the efferent nerve activity. The electrode needs to be placed on a peripheral nerve 15 that contains afferent nerve fibres innervating mechanoreceptors located in the bladder. Possible locations for the electrode are therefore: intradural dorsal sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches. An alternative method to detect a bladder contraction is to record from the efferent nerve fibres that innervate the detrusor muscle. An increase in the efferent signal results in a detrusor contraction so an increased efferent signal indicates a detrusor contraction. Possible locations for the electrode to record efferent signals from peripheral nerve 15 are: intradural ventral sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches.--

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On page 9, please replace the second full paragraph beginning at line 22, with the following amended paragraph:

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--Fig. 3 shows in detail the elements of the invention.

B/3 A Bladder-bladder 31 with a closing mechanism comprising a sphincter 32 together with the innervating peripheral nerves, which comprises ~~34~~ intradural dorsal sacral root 34, intradural ventral sacral root 35, extradural sacral root 36, ~~Preganglionic Pelvic~~ preganglionic pelvic nerve 37, ~~Postganglionic~~ postganglionic pelvic nerve 38 and ~~Pudendal~~ pudendal nerve 39. In addition, the dorsal penile/clitoral nerve 40 is shown. These nerves relay information to and from the spinal cord 33. A recording electrode 41 senses information from the nerves 37, and electrical information is transmitted through an electrode lead 43 to a signal processing unit 44, which is connected to a stimulator 45. ~~Signal from The~~ ~~signal from the~~ stimulator 45 is transmitted through an electrode lead 43 to a stimulation electrode 42, which stimulates nerve 40.--

B/4 On page 9, after the last line, please insert the following paragraph:

--The invention being thus described, it will be apparent that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the invention, and all such modifications as would be recognized by one skilled in the art are intended to be included within the scope of the following claims.--

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Please delete page 10 with the listing of reference elements in its entirety.